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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/245,603 02/05/99 CURIEL

D D6080

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HM12/0228

EXAMINER

PARAS, JR., P

ART UNIT

PAPER NUMBER

1632

DATE MAILED:

02/28/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/245,603

Applicant(s)

CURIEL ET AL.

Examiner

Peter Paras, Jr..

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 October 2000.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4,6-9,11-16,18-20,22 and 23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4,6-9,11-16,18-20,22 and 23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

Applicants' Amendment received on October 17, 2000 (Paper No. 6) has been entered. Claims 1-2, 6-7, 9, 11, 16, 18-19, and 22 have been amended. Claims 5, 10, 17, and 21 have been cancelled. Claims 1-4, 6-9, 11-16, 18-20, and 22-23 are pending and are currently under examination.

Prior rejections not made of record in the instant Office action have been withdrawn in view of Applicants amendments to the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6-7, 16, 18-20, and 22 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an adenovirus comprising an insertion of a ligand comprising the sequence CDCRGDCFC or the FLAG octapeptide into the HI loop of the fiber protein and a method of using the said adenovirus for methods *in vitro*, does not reasonably provide enablement for an adenovirus comprising any modification of the HI loop of the fiber protein and methods of using the virus in methods *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The rejection of claims 1-4, 6-7, 16, 18-20, and 22 is maintained for the reasons advanced in Paper No. 4 on pages 2-5 of the Office action.

Applicant's arguments have been fully considered but they are not persuasive. Applicants argue that sufficient information is available to one of skill in the art to insert a ligand into the loop regions of the fiber protein without causing significant changes to the folding/binding of the fiber protein as Wickham et al disclose which residues are important in the fiber knob for binding/folding. See Amendment pages 5. Applicants assert that several examples described by the specification demonstrated enhanced gene transfer to primary tumor cells. See Amendment page 7.

In response, the Examiner asserts that while Wickham et al discloses which amino acid residues are important for secondary structure in the fiber knob protein, the claims as written are directed to a fiber gene modified by introducing any ligand into the HI loop domain of the fiber knob. It is maintained the effect of any modification introduced into the HI fiber loop region is unpredictable with respect to trimerization, and folding/binding properties. The examiner asserts that the examples described by the specification taught specific modifications of the HI loop for enhancement of gene transfer. It remains unpredictable if modification introduced into the HI loop domain of the fiber knob can enhance gene transfer into primary tumor cells. It is further maintained that determination of the effects of particular modifications are not predictable until they are actually made and used, resulting in a trial and error situation. See pages 2-5 of the Office action. Accordingly, for the reasons of record and as discussed in the preceding paragraphs the rejection under 1-4, 6-7, 16, 18-20, and 22 is maintained.

Claims 9, 11-15, and 23 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The rejection of claims 9, 11-15, and 23 is maintained for the reasons advanced in Paper No. 4 on pages 2-5 of the Office action.

Applicant's arguments have been fully considered but they are not persuasive. Applicants assert that claim 9 has been amended to recite an adenovirus of the present invention further comprising a herpes simplex virus-thymidine kinase gene and that claim 11 recites a method of using the virus of claim 9 and ganciclovir to kill tumor cells in an individual. Applicants also assert that treatment of cancer in a patient by administration of an adenovirus comprising HSV-TK and ganciclovir is a standard treatment procedure that is currently used in a number of gene therapy trials. See pages 7-8 of the Amendment

In response, the Examiner asserts that any modification of the HI loop encompassed by the claims is unpredictable with respect to trimerization, folding/binding properties, and cell entry. The art of gene therapy was unpredictable at the time of filing of the claimed invention and remains so hereafter. As Applicants' specification provides no working examples that demonstrate enhanced cell uptake of the claimed adenovirus comprising any modification of the HI loop that correlates to killing of any tumor cell the rejection of claims 9, 11-15, and 23 under 35 U.S.C. 112,

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first paragraph is maintained for the reasons of record and as discussed in the preceding paragraphs.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13-15 stand rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The rejection of claims 13-15 under 35 U.S.C. 112, second paragraph, is maintained for the reasons advanced in Paper No. 4 on pages 6-7 of the Office action.

Although Applicant's have traversed the rejection of claims 13-15 under 35 U.S.C. 112, second paragraph, no arguments have been presented as to how the claims are complete as written nor have the claims been amended. Accordingly, the rejection of claims 13-15 under 35 U.S.C. 112, second paragraph is maintained for the reasons of record.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application

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by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-4, 6-9, 16, 18-20, and 23 stand rejected under 35 U.S.C. 102(e) as being anticipated by Wickham et al. The prior rejection of claims 1-4, 6-9, 16, 18-20, and 23 is maintained for the reasons of record advanced in Paper No. 4 on pages 6-7 of the Office action.

Applicant's arguments have been fully considered but they are not persuasive. Applicants argue that Wickham et al did not teach or suggest a modified adenovirus that enhances gene transfer to primary tumor cells.

In response, the Examiner asserts that Wickham et al is replete with recitations of a modified adenovirus that enhances gene transfer in cells, including tumor cells. See col. 8 lines 55 and 66, col. 27, Table 3 in col. 36, col. 13-14 as noted in the previous Office action on pages 6-7, for example. Accordingly, for the reasons of record and as discussed in the preceding paragraph claims 1-4, 6-9, 16, 18-20, and 23 stand anticipated by Wickham et al.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within

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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

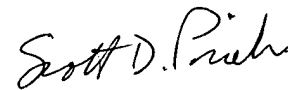
Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached at 703-305-6608. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to Kay Pinckney whose telephone number is (703) 305-3553.

Peter Paras, Jr.

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SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER